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(54) Title: DISEASE RISK ESTIMATING METHOD USING SEQUENCE POLYMORPHISMS IN A SPECIFIC REGION OF CHROMOSOME 19

(57) Abstract: The present invention provides methods and compositions for identifying human subjects with an increased risk of having or developing disease. In particular, this invention relates to the identification and characterization of polymorphisms in the human chromosome 19q, the region r located approximately 19q13.2-3 correlated with increased risk of developing disease, in particular cancer and the responsiveness of a subject to various treatments for cancer. An allele in the r region can be identified as correlated with an increased risk of developing disease, in particular cancer, the prognosis of developed disease, in particular cancer, and responsiveness to disease treatment, in particular cancer treatment on the basis of statistical analyses of the incidence of a particular allele in individuals diagnosed with disease, in particular cancer. The invention further relates to probes and kits comprising the probes useful in the diagnostic.



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C. DOCUM	ENTS CONSIDERED TO BE RELEVANT			
Category °	Citation of document, with indication, where appropriate, of the	ne reluvant passages		Relevant to claim No.
P,X	YIN JIAOYANG ET AL: "Multiple nucleotide polymorphisms on his chromosome 19q13.2-3 associated for basal cell carcinoma." CANCER EPIDEMIOLOGY BIOMARKER PREVENTION, vol. 11, no. 11, November 2007 pages 1449-1453, XP002261348 ISSN: 1055-9965 (ISSN print) abstract, table 1, 2 & 4; discontinuous de la companya del companya del companya de la companya del companya del companya de la c	uman e with risk S AND 2 (2002-11),		1-22, 24-35,37
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* Special ce "A" docum conside "E" earlier filing ("L" docum which citatio "O" docum "O" docum	ent defining the general state of the last which is not dered to be of particular relevance document but published on a rater the international date ent which may throw doubts on priority claim(s) or is cited to establish the publication date of another or or other special reason (as specified) sent referring to an oral disclosure, use, exhibition or means ent published prior to the international filing date but than the priority date claimed	or priority date a cited to understa hvention "X" document of parti- cannot be considered involve an invention "Y" document of parti- cannot be considered to com- menta, such com- in the art.	bliahed after the internal not in conflict with it mid the principle or the cular relevance; the claim of the principle of the cular relevance; the claim of the cular relevance; the claim of the coular relevance; an invabled with one or more obtained to being obvious or of the same patent fi	ne application but ony underlying the simed invention as considered to comment is taken alone arrivention antive step when the e other such docu- s to a person skilled
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C,(Continu	ation) DOCUMENTS CONSIDERED TO BE RELEVANT	
Category *	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to daim No.
P,X	NEXO BJORN A ET AL: "A specific haplotype of single nucleotide polymorphisms on chromosome 19q13.2-3 encompassing the gene RAI is indicative of post-menopausal breast cancer before age 55." CARCINOGENESIS (OXFORD), vol. 24, no. 5, May 2003 (2003-05), pages 899-904, XP002261349 ISSN: 0143-3334 the whole document	1-35,37
P,X	ROCKENBAUER ESZTER ET AL: "Association of chromosome 19q13.2-3 haplotypes with basal cell carcinoma: Tentative delineation of an involved region using data for single nucleotide polymorphisms in two cohorts" CARCINOGENESIS (OXFORD), vol. 23, no. 7, July 2002 (2002-07), pages 1149-1153, XP002261350 ISSN: 0143-3334 the whole document	1-35,37
P,X	YIN JIAOYANG ET AL: "Twelve single nucleotide polymorphisms on chromosome 19q13.2-13.3: Linkage disequilibria and associations with basal cell carcinoma in Danish psoriatic patients." BIOCHEMICAL GENETICS, vol. 41, no. 1-2, February 2003 (2003-02), pages 27-37, XP002261351 ISSN: 0006-2928	31-35,37
P,A	tables I,II	1-30
P,X	BERGAMASCHI DANIELE ET AL: "iASPP oncoprotein is a key inhibitor of p53 conserved from worm to human." NATURE GENETICS, vol. 33, no. 2, February 2003 (2003-02), pages 162-167, XP002272762 ISSN: 1061-4036 (ISSN print) page 163, column 2, paragraph 3 page 166, column 1, paragraph 1	36
X	SHEN M RICHARD ET AL: "Nonconservative amino acid substitution variants exist at polymorphic frequency in DNA repair genes in healthy humans" CANCER RESEARCH, vol. 58, no. 4, 15 February 1998 (1998-02-15), pages 604-608, XP002261352 ISSN: 0008-5472 table 1	31-35,37
	-/	
1		·

Form PCT/ISA/210 (continuation of second sheet) (January 2004)

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	Allon) DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, whore appropriate, of the relevant passages	Relevant to claim No.
Category °	Citation of document, with indication, whore appropriate, or the relevant passages	Tisiavara to ejajiji No.
X	VOGEL ULLA ET AL: "Polymorphisms of the DNA repair gene XPD: Correlations with risk of basal cell carcinoma revisited" CARCINOGENESIS (OXFORD), vol. 22, no. 6, June 2001 (2001-06), pages 899-904, XP002261353 ISSN: 0143-3334 page 900, column 1, paragraph 3 paragraph 7	31-35,37
Α	page 903, column 1, paragraph 4	1-35,37
x	DYBDAHL MARIANNE ET AL: "Polymorphisms in the DNA repair gene XPD: Correlations with risk and age at onset of basal cell carcinoma" CANCER EPIDEMIOLOGY BIOMARKERS AND PREVENTION, vol. 8, no. 1, January 1999 (1999-01), pages 77-81, XP002261354 ISSN: 1055-9965 page 78, column 1, paragraph 6	31-35,37
X	WO 95 16791 A (UNIV MCGILL ;POIRIER JUDES (CA)) 22 June 1995 (1995-06-22) claim 19	31-35,37
×	CHEN PENGCHIN ET AL: "Association of an ERCC1 polymorphism with adult-onset glioma" CANCER EPIDEMIOLOGY BIOMARKERS AND PREVENTION, vol. 9, no. 8, August 2000 (2000-08), pages 843-847, XP002261355 ISSN: 1055-9965	30
A	page 846, column 1, paragraph 4 abstract	1-35,37
X	YANG JIAN-PING ET AL: "Identification of a novel inhibitor of nuclear factor-kappaB, RelA-associated inhibitor" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 22, 28 May 1999 (1999-05-28), pages 15662-15670, XP002261356 ISSN: 0021-9258 the whole document	30
Α		1-35,37
x	EP 1 146 054 A (ONO PHARMACEUTICAL CO) 17 October 2001 (2001-10-17) abstract; claim 10 -/	36

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	citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.
Category *	Citation of document, with indication, where appropriate, or the relevant passages		Time varie to cizin No.
A	BREWSTER A M ET AL: "The association between polymorphisms in the xeroderma pigmentosum group D gene and risk of breast cancer" AMERICAN JOURNAL OF EPIDEMIOLOGY, vol. 153, no. 11 Supplement, 1 June 2001 (2001-06-01), page S198 XP002261357 Joint Meeting of the Society for Epidemiologic Research, American College of Epidemiology, Epidemiol; Toronto, Canada; June 13-16, 2001 ISSN: 0002-9262 the whole document		1-35,37
A	BUTKIEWICZ DOROTA ET AL: "Genetic polymorphisms in DNA repair genes and risk of lung cancer" CARCINOGENESIS (OXFORD), vol. 22, no. 4, April 2001 (2001-04), pages 593-597, XP002261358 ISSN: 0143-3334 abstract; table II; discussion		1-35,37
			·

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ation on patent family members

Internal Application No PC170K 03/00448

Patent document clted in search report		Publication date		Patent family member(s)	Publication date
WO 9516791	Α	22-06-1995	CA AU WO	2111503 A1 1189395 A 9516791 A1	16-06-1995 03-07-1995 22-06-1995
EP 1146054	Α	17-10-2001	EP US WO JP US	1146054 A1 6582933 B1 0032628 A1 2000224993 A 2003148396 A1	17-10-2001 24-06-2003 08-06-2000 15-08-2000 07-08-2003

Form PCT/ISA/210 (patent family annex) (January 2004)